

The University of Chicago

THE EFFECT OF A DIETARY SUPPLEMENT
ON OSSIFICATION OF THE BONES OF
THE WRIST IN INSTITUTION
CHILDREN

A DISSERTATION SUBMITTED TO THE
FACULTY OF THE DIVISION OF THE
BIOLOGICAL SCIENCES IN CANDIDACY FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF HOME ECONOMICS
AND HOUSEHOLD ADMINISTRATION

1937

By
VERA MacNAIR

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EFFECT OF A MILK SUPPLEMENT ON THE PHYSICAL STATUS OF INSTITUTIONAL CHILDREN

II. OSSIFICATION OF THE BONES OF THE WRIST

VERA MacNAIR, PH.D.

ROCK HILL, S. C.

Ossification in the wrist and forearm has been widely used by anatomists, educators and other investigators as an index of anatomic age. As such, it has been correlated with mental age, the intelligence quotient and other factors, and important conclusions have been drawn from the findings. Only rarely has the suggestion been made that this index might be modified by the state of nutrition, although it seems almost self evident that any prolonged deficiency or marked improvement in the diet would have an appreciable effect on development of bone.

The present study was prompted by the desire to study this question under experimental conditions. An excellent opportunity was presented to do this in connection with a larger study, which was being carried out in a children's institution.¹ The purpose of the project was to determine whether an increase in the amount of milk consumed to make a total of approximately 1 quart (946 cc.) daily per child would produce any measurable improvement in the physical status of the children in a year's time and whether any advantage could be demonstrated for irradiated over nonirradiated milk.

EXPERIMENTAL PROCEDURE

Subjects.—As indicated in a preceding article,¹ the subjects comprised all the residents in an institution caring for approximately 150 children. The ages ranged from 1 to 15 years, but the large majority of the children were of grade school age. At the beginning of the experimental year three groups were set up; they were as nearly alike as possible as to age, sex and nutritional status, as judged by height, weight and condition of the teeth. The control group continued to receive the

From the Department of Home Economics of the University of Chicago.

The expenses of this investigation were defrayed in part by the Irradiated Evaporated Milk Institute.

1. Roberts, L. J.; Blair, R.; Lenning, B., and Scott, M.: Effect of a Milk Supplement on the Physical Status of Institutional Children: I. Growth in Height and in Weight, *Am. J. Dis. Child.* **56**:287 (Aug.) 1938.

institutional diet; one group was given an additional pint (473 cc.) equivalent of evaporated milk, and the third group was given an equal amount of irradiated evaporated milk.

Area Chosen for Study.—The wrist was chosen as the portion of the skeleton in which to follow osseous development. This is a justifiable procedure, since ossification of the bones of the wrist has been shown by numerous workers to be representative of development in other centers (Pryor,² Rotch,³ Baldwin, Busby and Garside,⁴ Wallis⁵). This does not mean that development will be precisely the same throughout the body but merely that if ossification is accelerated or retarded in the wrist it will be correspondingly accelerated or retarded elsewhere. In comparing the progress of these three groups of children it seems reasonable, then, to assume that the rate of development of the carpal bones can be considered indicative of the stage of development throughout the skeleton. Both Todd⁶ and Wallis⁵ have suggested that other centers of ossification, the knee, for example, may be better indicators at certain stages; but for the entire period of growth from birth to maturity, development of the carpal bones and of the epiphyses of the hand and wrist provides a complete scale, correlating with that of the epiphyses elsewhere. Two additional reasons for using the hand were the greater practical ease of taking roentgenograms of this area and especially the fact that the norms for skeletal development now available for comparison are based on measurement of these centers of ossification.

Roentgenograms.—Roentgenograms of the right hands were taken with a Ritter portable x-ray machine. Great care was exercised to have the hands and arms in a uniform position in order that all roentgenograms would be strictly comparable. In each case the hand and the greater part of the forearm were placed on a table, with the hand in the roentgen field and against the film holder. The fingers were held together; the thumb was slightly and naturally extended. The middle finger, the third metacarpal bone and the long axis of the forearm were in alinement. With this position, the upper surface of the lower part of the forearm was practically parallel with the surface of the table. Even slight rotation changes the profile of the radial and ulnar epiphyses and also the position and visible area of the carpal bones. The position described gives the broadest shadows of these

2. Pryor, J. W.: Development of the Bones of the Hand, Bull. State Coll. Kentucky, June 1905; Some Observations on the Ossification of Bones of the Hand, Bull. Univ. Kentucky **8**:67, 1916; Roentgenographic Investigation of the Time Element in Ossification, Am. J. Roentgenol. **29**:798 (June) 1933.

3. Rotch, T. M.: Roentgen Ray Methods Applied to the Grading of Early Life, Phys. Educ. Rev. **15**:396, 1910.

4. Baldwin, B. T.: Physical Growth of Children from Birth to Maturity, Iowa City, University of Iowa Press, 1921, chap. 7. Baldwin, B. T.; Busby, L. M., and Garside, H. V.: Anatomic Growth of Children, Iowa City, University of Iowa Press, 1928, p. 88.

5. Wallis, R. S.: How Children Grow, Iowa City, University of Iowa Press, 1931, p. 137.

6. Todd, T. W.: (a) The Skeleton, in Growth and Development of the Child: II. Anatomy and Physiology, White House Conference on Child Health and Protection, New York, Century Company, 1932, pp. 46-90; (b) Roentgenographic Appraisalment of Developmental Growth in the Skeleton, in Growth and Development of the Child: IV. Appraisalment of the Child, *ibid.*, pp. 258-285; (c) Bodily Expression of Human Growth and Welfare, Science **82**:181 (Aug. 30) 1935.

bones. In the case of a few children, notably several extremely thin ones, whose wrists were difficult to put into the correct position, the arm and hand were held in place during the exposure. After development, all roentgenograms were examined carefully, and any doubtful ones were retaken. By this method roentgenograms were taken of all children at the beginning and at the end of the experimental year.

Measuring the Progress in Osseous Development.—A number of methods of determining the stage of osseous development were available, several, as that of Prescott^{6d} having norms, derived from measurements for large numbers of children. The two chosen for use in this study were the Flory inspectional age scale⁷ and the Carter index, or ossification ratio.⁸ The Flory scale was used primarily for matching children in the several groups at the beginning. This is an inspectional age scale which measures qualitative as well as quantitative aspects of development. The inspectional method was the earliest one to be used for expressing anatomic age. Pryor, in 1905, prepared a chronologic time table for the appearance of the epiphyses and the development of the carpal bones. As early as 1908 Rotch suggested that a series such as that of Pryor might be of considerable value in assessing anatomic age. He proposed using the development of the carpal bones and of the epiphyses of the radius and the ulna for the period from infancy to puberty and the ossification and union of epiphyses of the radius, the ulna, the metacarpal bones and, in succession, the phalanges for the period from adolescence to maturity. Woodrow and Lowell⁹ and Smith¹⁰ also described the successive changes of the carpal bones and epiphyses in the growing hand, but they did not set up norms that could be used by other workers. Todd described more specifically¹¹ a time table for the appearance of the ossification centers, rate of spread of ossification and union of epiphyses not only in the bones of the hand and forearm but also in those of the knee, ankle and foot.

Flory extended and systematized descriptions for the inspectional method as applied to one of these areas, that is, to the hand and forearm.⁷ He used for this purpose approximately 3,000 roentgenograms of the hands of children of the University of Chicago Laboratory Schools and of other children of similar socio-economic status.¹² From these records he chose a typical roentgenogram of the

6d. Prescott, D. A.: *Determination of Anatomical Age in School Children and Its Relation to Mental Development*, Cambridge, Harvard University Press, 1923.

7. Flory, C. D.: *Osseous Development in the Hand as an Index of Skeletal Development*, Monograph 3, Society for Research in Child Development, Washington, D. C., National Research Council, 1936, p. 41.

8. (a) Freeman, F. N., and Carter, T. M.: *A New Measurement of the Development of the Carpal Bones and Its Relation to Physical and Mental Development*, J. Educ. Psychol. **15**:257, 1924. (b) Carter, T. M.: *Technique and Devices Used in Radiographic Study of the Wrist Bones of Children*, *ibid.* **17**:237, 1926.

9. Woodrow, H. H.: *Brightness and Dullness in Children*, Philadelphia, J. B. Lippincott Company, 1919, pp. 97-122. Woodrow, H. H., and Lowell, F.: *Various Indices of Anatomic Age*, *Pedagog. Semin.* **29**:1, 1922.

10. Smith, H. W., and Rotch, T. M.: *Method of Roentgenographic Age Determination*, U. S. Nav. M. Bull. **7**:20, 1913.

11. Todd.^{6a, b}

12. One hundred in each age and sex group for the ages from 8 to 17 years; from 67 to 100 for the ages from 5 to 7 years and, from 30 to 36 for the age of 4 years.

right hand for each age and sex from birth to 20 years and then prepared a detailed description of the characteristics most typical of each stage of development. These descriptions concern not only carpal bones and radial and ulnar epiphyses but all epiphyses in the hand as well. They take into account, therefore, all types of changes which various authors have considered significant in assessing development. These typical roentgenograms together with the detailed descriptions constitute a series of norms for skeletal development. By comparison with these standards a particular child may be given an inspectional age, namely, that of the roentgenogram to which his own mostly closely corresponds. This scale is obviously to a considerable extent subjective and has therefore some of the disadvantages of any subjective measure. Flory has expressed the belief, however (and experience in this study has confirmed his belief), that when a roentgenogram may be directly compared with the standard roentgenogram typical of each age as well as with the accompanying description, much of the subjectivity is ruled out. For showing qualitative as well as quantitative growth the method has decided advantages.

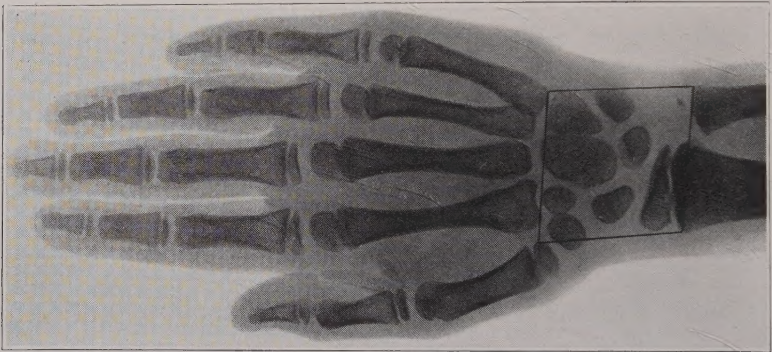


Fig. 1.—Roentgenogram of the hand of a girl 7 years and 5 months old, showing the outline of the area circumscribed for the Carter quadrilateral.

The Carter index was used for comparing the rate of ossification in the three dietary groups. This method was first described by Freeman and Carter, in 1924.^{8a} It relates the sum of the areas of the shadows of the carpal bones and of the epiphyses of the radius and the ulna as actually measured by a planimeter to the area of the wrist (fig. 1), that is, it relates the area already ossified to the area to be ossified.

$$\frac{\text{Ossified area}}{\text{Area of carpal quadrilateral}} = \text{Ossification ratio}$$

Norms of osseous development for each age and sex were prepared by this method from examination of roentgenograms of children in the University of Chicago Laboratory Schools. Flory has recently revised these norms (using children in the same school) by greatly extending the number of children. These ratios make it possible to express the degree of development of the bones of the wrist in terms of its relation to the norm for age and sex and to compare children objectively with each other in this respect. Successive roentgenograms of the same child will show his increments of osseous growth, and these increments may be compared with those to be expected for his age, as indicated by the standards, as well as with those of other children. The statistical data here presented are

based on the Carter method of determining anatomic development. It was chosen because it is an objective method derived from a study of large numbers of children of a similar socioeconomic group, the units are small, the ratios are obtained by direct measurement and differences in growth are apparent in figures of appreciable size.

The Flory inspectional age scale was used and was found invaluable in placing children in order of developmental age and in matching children for the three groups. Partners were thus chosen on the basis of qualitative development in the whole hand as well as quantitative growth. Differences due to experimental procedure were determined by measuring the area of the wrist at the beginning and at the end of the year; these are expressed as differences between the increments of osseous growth so obtained.

In making the measurements for the present study a film was placed on a specially constructed light-box, and a polar planimeter was used in measuring the areas of the carpal bones and of the quadrilateral of the wrist for the Carter index. The planimeter is an ingenious device for measuring irregular areas of plane surfaces (as in maps). The polar planimeter, as here used, consists of two arms (the pole arm and the tracer arm) and the carriage. The tracer arm runs on a measuring wheel the movement of which is directly proportional to the area of the plane surface circumscribed by the tracer point. An attached vernier permits reading to the nearest hundredth of a square inch (0.06 sq. cm.). The area is recorded as the difference between the initial and the final reading. Measurements of the magnitude of the carpal areas can be duplicated easily by different trained observers and by the same person rereading the roentgenograms after an interval of several months.

In our study every precaution was taken to secure accurate measurements. All films were measured by the same person (V. MacN.), who acquired facility by checking with 2 experienced persons and who repeatedly tested her consistency and accuracy by rechecking her previous measurements. In order to minimize errors in measuring small bones or very irregular ones, the boundaries of these were traced three times, and the sum obtained was divided by 3. All measurements of the quadrilateral were also checked. As a final check on both measurer and recorder, each completed set of measurements on a roentgenogram was scanned for reasonableness of areas as judged by inspection of the bones and their relative size. To rule out any possible effect of the subjective element, all measurements were made and the indexes were computed and recorded with no knowledge on the part of the worker as to whose roentgenogram was being evaluated.

In order to determine the status of a particular child, it was necessary to interpolate, in the center scale, index values or ossification ratios for months of the year. The roentgenograms were taken for all children at the beginning and at the end of the experimental year and only incidentally near birthdays. It was necessary to be able to compare the figures for a child directly, whatever the number of months since his last birthday, with the standards. The interpolations made such comparisons possible.

Matching the Groups.—Although the initial roentgenograms were taken at the beginning of the study, almost simultaneously with other measurements, they could not be used in setting up the three groups for the study. This was true because, first, the technic of measuring and interpreting the films had to be mastered and, second, the measurements had to be made, several months elapsing before these tasks were accomplished. The three groups therefore had to be set up on other bases, as already described, and the supplementation was started long before the initial roentgenograms had been measured. There remained of these three groups

at the end of the study 35 controls, 37 children given milk and 36 given vitamin D milk, a total of 108. For some comparisons this initial grouping was used to assess the progress in anatomic development with which this article is concerned. It was clear, however, that a better comparison could be made for children matched on the basis of their initial anatomic age. After the first roentgenograms were developed and measured, therefore, the children were rematched as well as possible by stage of osseous development, all children being kept, of course, in their original dietary groups.

In selecting the new sets the Flory inspectional age was the chief criterion used; it was fortified by the Carter index and the chronologic age. Trios were formed by selecting from each of the original dietary groups a child matching those from the other 2 in skeletal months by the Flory standard, that is, a child at the same stage of development toward the mature form. The partners also were selected so that the age according to the Carter index and the chronologic age were the same or nearly so. In most cases all three criteria showed the ages of the 3 matched children to be within six months of each other; in others the ages were the same according to two criteria (one of them the Flory inspectional age) and were not far apart by the third. The Flory standard emphasizes develop-

TABLE 1.—*Comparison of the Three Matched Dietary Groups at the Beginning of the Experiment*

Group	Mean Chronologic Age		Mean Carter Index		Flory Inspectional Age, Mean Skeletal Months	
	Boys	Girls	Boys	Girls	Boys	Girls
Control.....	10.30	9.00	62.3	66.6	113	98
Plain milk.....	10.00	9.10	61.1	66.4	112	100
D milk.....	10.25	8.80	63.0	65.4	113	99

ment; the Carter index, growth in size of the ossified area. When these and the chronologic age were similar for a set of 3 children, it was judged that the trio were as nearly as possible in the same phase of growth at the beginning of the year. There were 24 sets of 3 children who could be thus matched and who remained till the end of the year. That the three groups made up from these matched trios were similar in osseous development is shown in table 1. The Carter index and the Flory inspectional age are remarkably alike for the matched dietary groups, and chronologic age, which was given less consideration in matching, agrees within a third of a year. A comparison of the progress of these three groups during the year should then be the best test of the effect of the dietary supplement on anatomic development.

RESULTS

As a result of obtaining measurements by means of the procedures which have been described, there were available for comparison Carter ossification ratios for 108 children at the beginning and at the end of the year. This includes the selected group of 72 children, 24 in each dietary group, who were initially matched as to sex and stage of osseous development. It is now of interest to examine the progress made by these children in a year, to determine whether there was any significant

TABLE 2.—*Deviation from Carter Indexes for all Matched Children at the Beginning and at the End of the Study and Changes During the Year in Relation to the Mean Index for Age and Sex and in Relation to Expected Gains*

No.	Sex	Carter Index at Beginning	Mean Age	Deviation at Beginning		Carter Index at End	Mean Age	Deviation at End		Changes in Deviation from Mean for Age		Gain in Score for Year		Percentage of Expected Gain
				Points	Percentage			Points	Percentage	Points	Percentage	Actual	Expected	
Control group														
1	F	19	32	-13	-41	24	39	-15	-39	-2	+2	5	7	71
2	F	51	62	-11	-18	60	72	-12	-17	-1	+1	9	10	90
3	F	59	65	-6	-9	75	76	-1	-1	+5	+8	16	11	146
4	F	95	86	+9	+11	98	94	+4	+4	-5	-6	3	8	38
5	F	73	89	-16	-18	81	97	-16	-16	0	+2	8	8	100
6	F	80	96	-16	-17	91	103	-12	-12	+4	+5	11	7	157
7	F	89	96	-7	-7	94	102	-8	-8	-1	-1	5	6	83
8	M	24	27	-3	-11	29	31	-2	-6	+1	+5	5	4	125
9	M	41	45	-4	-9	46	53	-7	-13	-3	-4	5	8	63
10	M	37	55	-18	-33	42	63	-21	-33	-3	0	5	8	63
11	M	41	60	-19	-32	49	69	-20	-29	-1	-3	8	9	89
12	M	61	63	-2	-3	63	71	-8	-11	-6	-8	2	8	25
13	M	57	59	-2	-3	65	69	-4	-6	-2	-3	8	10	80
14	M	67	70	-3	-4	71	77	-6	-8	-3	-4	4	7	57
15	M	66	65	+1	+2	72	73	-1	-1	-2	-3	6	8	75
16	M	73	76	-3	-4	76	85	-9	-11	-6	-7	3	9	33
17	M	82	87	-5	-6	100	96	+4	+4	+9	+10	18	9	200
18	M	79	89	-10	-11	78	98	-20	-20	-10	-9	-1	9	-11
19	M	86	94	-8	-8	87	101	-14	-14	-6	-6	1	7	14
20	M	95	106	-11	-10	99	110	-11	-10	0	0	4	4	100
21	M	23	35	-12	-34	31	44	-13	-30	-1	+4	8	9	89
22	M	48	67	-19	-28	52	74	-22	-30	-3	-2	4	7	57
23	M	77	96	-19	-20	82	102	-20	-20	-1	0	5	6	83
24	M	162	104	-2	-2	104	108	-4	-4	-2	-2	2	4	50
Total		1,525	1,724	-199		1,669	1,907	-238		-39		144	183	
Group receiving plain milk														
1	F	28	35	-7	-20	32	43	-11	-26	-4	-6	4	8	50
2	F	50	63	-13	-21	59	73	-14	-19	-1	+2	9	10	90
3	F	58	70	-12	-17	67	79	-12	-15	0	+2	9	9	100
4	F	90	103	-13	-13	100	106	-6	-6	+7	+7	10	3	333
5	F	73	94	-16	-17	100	101	-1	-1	+15	+16	22	7	314
6	F	76	78	-2	-3	86	87	-1	-1	+1	+2	10	9	111
7	F	85	84	+1	+1	90	92	-2	-2	-3	-3	5	8	63
8	M	18	25	-7	-28	24	30	-6	-20	+1	+8	6	5	120
9	M	33	42	-9	-21	37	50	-13	-26	-4	-5	4	8	50
10	M	42	52	-10	-19	55	60	-5	-8	+5	+11	13	8	162
11	M	46	54	-8	-15	56	62	-6	-10	+2	+5	10	8	125
12	M	50	71	-21	-30	60	78	-18	-23	+3	+7	10	7	143
13	M	58	63	-5	-8	67	71	-4	-6	+1	+2	9	8	112
14	M	67	71	-4	-6	70	78	-8	-10	-4	-4	3	7	43
15	M	51	71	-20	-28	58	78	-20	-26	0	+2	7	7	100
16	M	60	82	-22	-27	76	92	-16	-17	+6	+10	16	10	160
17	M	81	94	-13	-14	85	101	-16	-16	-3	-2	4	7	57
18	M	79	73	+1	+1	85	88	-3	-3	-4	-4	6	10	60
19	M	87	92	-5	-5	96	99	-3	-3	+2	+2	9	7	129
20	M	101	100	+1	+1	105	105	0	0	-1	-1	4	5	80
21	M	23	30	-7	-23	26	35	-9	-26	-2	-2	3	5	60
22	M	52	49	+3	+6	58	57	+1	+2	-2	-4	6	8	75
23	M	99	106	-7	-7	108	110	-2	-2	+5	+5	9	4	225
24	M	91	99	-8	-8	102	104	-2	-2	+6	+6	11	5	220
Total		1,503	1,706	-203		1,702	1,879	-177		+26	+55	199	173	
Group receiving D milk														
1	F	29	35	-6	-17	33	43	-10	-23	-4	-6	4	8	50
2	F	50	63	-13	-21	61	72	-11	-15	+2	+6	11	9	122
3	F	54	61	-7	-12	67	71	-4	-6	+3	+6	13	10	130
4	F	95	101	-6	-6	99	105	-6	-6	0	0	4	4	100
5	F	70	86	-16	-19	81	94	-13	-14	+3	+5	11	8	138
6	F	83	77	+6	+8	93	86	+7	+3	+8	+1	0	10	9
7	F	77	89	-12	-14	99	97	+2	+2	+14	+16	22	8	275
8	M	21	28	-7	-25	25	32	-7	-22	0	+3	4	4	100
9	M	29	35	-6	-17	38	44	-6	-14	-3	-3	9	9	100
10	M	45	65	-20	-31	48	73	-25	-34	-5	-3	3	8	38
11	M	50	63	-13	-21	55	71	-16	-23	-3	-3	5	8	63
12	M	64	63	+1	+2	69	71	-2	-3	-3	-5	5	8	63
13	M	59	68	-9	-13	70	75	-5	-7	+4	+6	11	7	157
14	M	64	71	-7	-10	78	79	-1	-1	+6	+9	14	8	175
15	M	64	71	-7	-10	67	79	-12	-13	-5	-3	3	8	38
16	M	64	68	-4	-6	70	74	-4	-5	0	+1	6	6	100
17	M	81	97	-16	-17	85	102	-17	-17	-1	0	4	5	80
18	M	78	97	-19	-20	89	103	-14	-14	+5	+6	11	6	183
19	M	84	87	-3	-3	92	96	-4	-4	-1	-1	8	9	89
20	M	95	107	-12	-11	102	110	-8	-7	+4	+4	7	3	233
21	M	27	45	-18	-36	33	53	-20	-38	-2	-2	6	8	75
22	M	49	43	+6	+14	59	51	+8	+16	+2	+2	10	8	125
23	M	92	101	-9	-9	96	106	-10	-9	-1	0	4	5	80
24	M	102	101	+1	+1	113	106	+7	+7	+6	+6	11	5	220
Total		1,526	1,722	-196		1,722	1,893	-171		+25		196	171	

difference in rate of development between the groups receiving a supplement and the group not receiving one. The data obtained have been subjected to a number of comparisons. These have been made both for all the 108 children and for the 24 matched sets of 3 each. Since the matched sets provide the most reliable material, the comparisons for these will be given major consideration; the data for the 108 children will be used for confirmatory evidence.

TABLE 3.—*Percentage of Children in Matched Groups Having the Specified Relation to the Mean at the Beginning and at the End of the Year by Dietary Groups*

Group	Even with Mean or Above				Less Than 10 per Cent Below Mean				10 per Cent or More Below Mean			
	Beginning		End		Beginning		End		Beginning		End	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Control.....	2	8	2	8	10	42	7	29	12	50	15	63
Plain milk.....	4	17	2	8	6	25	10	42	14	58	12	50
D milk.....	4	17	4	17	4	17	9	38	16	67	11	46

TABLE 4.—*Change in Status in Relation to the Carter Mean During the Year by Dietary Groups*

Change in Carter Points	Control		Plain Milk		D Milk	
	No.	%	No.	%	No.	%
In more favorable relation to mean.....	4	17	12	50	11	46
By 5 or more points.....	2		6		4	
By 1-4 points.....	2		6		7	
In same relation to mean.....	2	8	2	8	4	17
In less favorable relation to mean.....	18	75	10	42	9	37
By 1-4 points.....	13		10		7	
By 5 or more points.....	5		..		2	

TABLE 5.—*Summary of Changes Made During the Year by Each of the Three Matched Dietary Groups Considered as a Unit*

Group	Deviation from Carter Mean				Total Points of Change in Devia- tion	Gain in Carter Points		Expected Gain		Actual Gain Over Expected Gain, %
	Beginning		End			Total Points	Mean	Total Points	Mean	
	Total Points	%	Total Points	%						
Control.....	-199	-11.5	-238	-12.5	-39	144	6.0	183	7.6	78.7
Plain milk.....	-203	-11.9	-177	-9.4	+26	199	8.3	173	7.2	115.0
D milk.....	-196	-11.4	-171	-9.0	+25	196	8.2	171	7.1	115.0

Change in Relation to the Carter Mean for Age.—In table 2 are given for each child the Carter ossification ratios at the beginning and at the end of the year, the deviation of these from the mean Carter index for age and sex and the gains made for the year. The first feature which strikes the eye is that with few exceptions all children

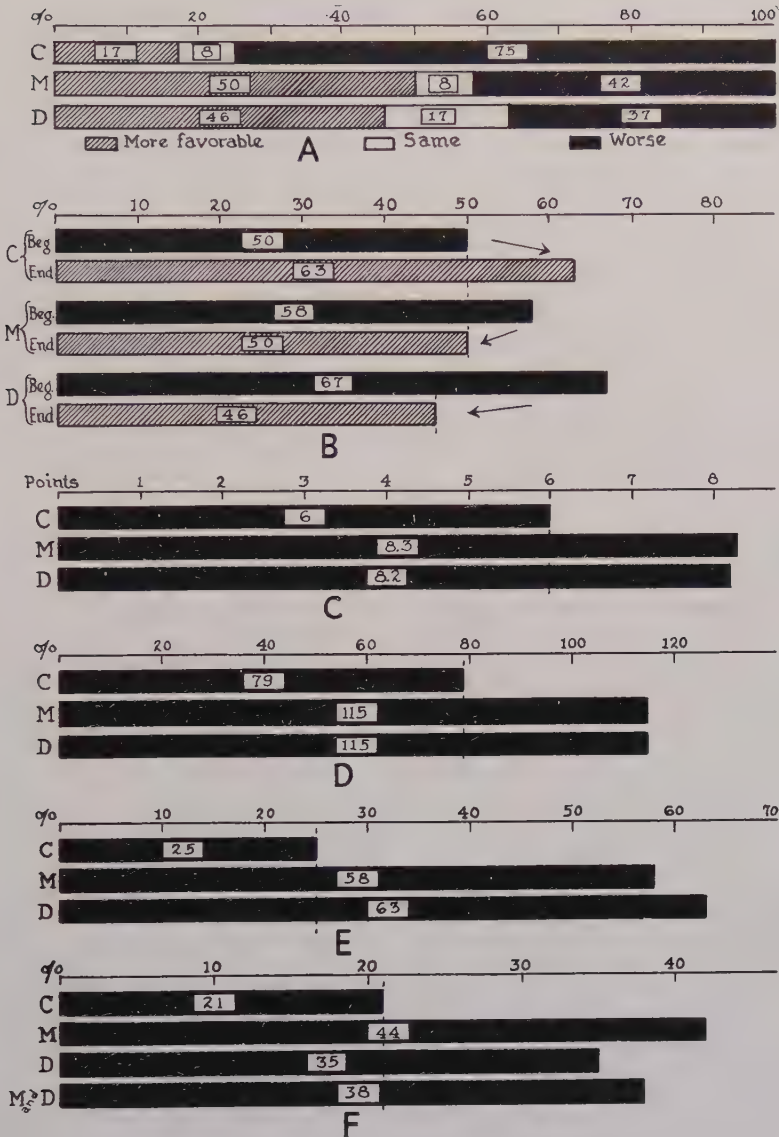


Fig. 2.—A, percentage of each group with a more favorable, the same or a worse relation to the norms at the end than at the beginning of the experimental year. B, percentage of each group 10 per cent or more below the norms at the beginning and at the end of the year. C, mean gain in Carter points. D, percentage of the expected gain made by each group. E, percentage of children in each group who made the expected gain or better. F, percentage of times in the matched trios a control child, one given milk and one given D milk, made the best gain during the year.

in all three groups were below the average in osseous development for their age, as judged by the Carter norms, both at the beginning and at the end of the year. Some of these negative differences were not large, but, as seen in table 3, over half the children at the outset were more than 10 per cent below the mean. The control group had some advantage in this respect, since only 50 per cent of these children, as compared with 58 and 67 per cent of the milk and of the D milk group, respectively, deviated as much as this from the average on their initial measurements. Taking each dietary group as a whole, however (table 5), the percentages of deviation from the mean were similar; 11.5 for the control, 11.9 for the plain milk and 11.4 for the irradiated milk group.

But how did the same groups stand at the end of the year? It is apparent from the summary in tables 3 to 5 that although all groups were still below the average the control group lost ground while the groups receiving a supplement reduced their deficits appreciably. Considering at first only whether individual children were better or worse off in this respect, it is found (table 4, fig. 2 *A*) that only 17 per cent of the control group improved their status, 8 per cent held their own and 75 per cent actually lost ground; that is, they were farther below the norms for their age at the end of the year than at the beginning. The milk groups fared better; 50 per cent of the children given plain milk and 46 per cent of those given D milk improved their status, and 42 and 37 per cent, respectively, were in less favorable relation to their means than they were at the beginning. When the size as well as the direction of these differences is considered, it is found that more children in the milk groups than in the control group have made gains of significant size. The percentage of children who reduced their deficits by 5 points or more was 8 for the control, 25 for the milk and 17 for the D milk group (table 4). The result of these larger gains by the milk groups is also seen in a shift in the percentage of children with negative deviations of 10 per cent or more from the standard. As seen in table 3 and figure 2 *B*, the percentage of children in the control group deviating as much as 10 per cent increased from 50 to 63, while it decreased from 58 to 50 for the plain milk group and from 67 to 46 for the D milk group.

A more precise method of comparison concerns the actual gain in the mean Carter ossification ratio made by each group during the year and its relation to the expected amount. In table 5 and figure 2 *C* it is seen that the mean advance in Carter points was 6 for the control, 8.3 for the plain milk and 8.2 for the D milk group. These differences of 2.3 and 2.2 Carter points in favor of the children given a supplement

are the equivalent of approximately one third of a year's expected quota. This will be referred to again in connection with the matched trios.

The same relation is shown when each group is considered as a unit and its total gains are compared with the expected gains by the Carter standards (table 5, fig. 2 *D*). The control group made but 79 per cent of its expected quota, while both the milk groups gained 115 per cent of their expected amounts. While the control group, then,

TABLE 6.—*Percentage of Matched Children Making the Specified Percentage of Expected Gains in Carter Points for the Year by Dietary Groups*

Amount of Gain	Control		Milk		D Milk	
	No.	%	No.	%	No.	%
100% of expected gain or more.....	6	25	14	58	15	62.5
200% or more.....	1		4		3	
100-199%.....	5		10		12	
Less than expected gain.....	18	75	10	42	9	37.5
Some gain.....	17		10		9	
No gain.....	1		..		..	

did not quite hold its own, the groups given a supplement stored a balance to their credit which helped to make up some of their arrears.

When individual children are considered (table 6, fig. 2 *E*) it is found that only 25 per cent of the controls as compared with 58 and 63 per cent, respectively, of the milk groups gained the expected amount or more during the year. Moreover, a larger number of the gains of 200 per cent of the expected or better were made by the children given milk, and the only case of failure of the carpal bones to keep up with the growth in the wrist was that of a control child.

TABLE 7.—*Number of Times in Twenty-Four Matched Trios the Specified Partner Made the Best Gain*

Child in Trio Making Best Gain	Number of Times	Percentage
Control.....	5.0	21.0
One or both partners receiving milk.....	19.0	79.0
Plain milk.....	10.5*	44.0
D milk.....	8.5*	35.0
Both partners receiving milk.....	9.0	37.5

* The milk partners showed the same values in one comparison.

One final comparison should be made on the basis of relative gains of individuals in the matched trios. This is obviously the most severe test of the efficacy of the supplement. Although the children in a given trio were closely alike at the outset as to their stage of osseous development and the dietary supplement was the only known variable that was introduced, it is obvious that many other factors which might affect

individuals in a group (such as colds or other illnesses or supplementary food brought by visitors) might obscure the effects of a specific experimental variable. It would hardly be expected, then, that in every trio the results would be sharply in favor of the children receiving the supplement, even though it may have had a favorable influence. It is of interest to note, nevertheless, how the partners in the several trios fared. Taking first the matter of relative gains, it is observed (table 7, fig. 2*F*) that in the 24 comparisons the control child was the best of the 3 in the gains he made 5 times while the child given plain milk was best $10\frac{1}{2}$ times and the one given D milk $8\frac{1}{2}$ times (the 2 partners given milk were the same in 1 comparison). That is, the control child was best in 21 per cent, the child given plain milk in 44 per cent and the child given D milk in 35 per cent of the comparisons. Both children given milk were better than the control partner in the trio 9 times, or in 37.5 per cent of the comparisons.

But the amount of the superiority should also be considered. This can best be determined by a comparison of the gain made on their means during the year by the partners in the matched trios. For example, in trio 4, table 2, the control child deviated from the mean for her age at the beginning by +9 points and at the end by +4 points. Her change in relation to the mean for her age was therefore -5 points. In similar manner, her partner who received plain milk is shown to have changed status by +7 points and the partner who received D milk by 0 point. A direct comparison can thus be made of the change in status during the year for the children given plain milk and D milk in each set with that of their control partners. For the previously described trio these differences are +12 points for the partner who received plain milk over the control and +5 points for the partner who received D milk over the control. The differences for partners in all 24 trios can be similarly obtained, and the average of these differences for each comparison can be determined (that is, between the partner who received plain milk and the control, the partner who received D milk and the control, and between the partners receiving milk).

By this method the mean of the differences between those receiving plain milk and the control partners is found to be 2.7 Carter points; the same difference is found for those receiving D milk and control partners. This is equivalent to 37 per cent of the mean expected gain for the year (7.3 Carter points) for the 72 children in the 24 trios. The difference between the plain milk and the D milk group is insignificant: 0.04 ± 0.9 point. It will be noted that this comparison of matched partners results in a larger difference between the groups given a supplement and the control group than was previously reported (table 5) as difference in mean gain. This apparent discrepancy is not real, since

the two procedures are measuring somewhat different factors. The previous figures for amount of superiority of the milk groups in osseous development (2.3 and 2.2 points) were obtained from average gains in the ossification ratio of the groups as a whole treated as random samples. This gives an approximate measure of the relative progress, which can be depicted graphically in a chart. By the latter comparison the ossification ratio is related to the Carter index for age and the expected gain for each partner. This increases the accuracy of the evaluation of the change, since it relates the change to a particular phase of growth. Still more important, it takes account of the fact that these were matched partners instead of children selected at random. This mean of the differences found from comparison of partners is therefore the most direct and accurate measure of real differences. The superiority of 2.7 Carter points for the partners who received milk over the controls obtained by this method is thus a more precise indication of the result of the experimental procedure than the 2.3 and 2.2 Carter points found for mean difference in "raw scores."

TABLE 8.—*Progress in Osseous Growth of One Hundred and Eight Children by Dietary Groups During the Experimental Year*

Item	Control	Milk	D Milk
Number of children.....	35	37	36
Percentage of children who are in a more favorable position in respect to the mean Carter index for age.....	26	54	41
Percentage of children 10 per cent or more below the mean:			
Beginning	54	43	61
End	60	38	47
Average gain for group:			
In Carter points.....	6.5	7.8	7.2
Percentage of expected gain.....	84	114	109
Percentage of children making expected gain or more.....	31	59	58

The differences between the milk groups and the control group are significant, since the ratio of the mean of the differences to its probable error is 3.23 for the group receiving plain milk over the control group and 3.47 for the group receiving D milk over the control group. This means that the chances are about thirty-three to one and fifty-five to one, respectively, that the differences are not due to chance and may be attributed to the milk supplement. Moreover, since all other differences found tend in the same direction, there is added assurance that the amount of the superiority of the groups given a supplement over the group not given one, that is, approximately one third of a year's expected quota of gain in ossification ratio, is significant.

Confirmatory Evidence from the Entire Group.—Though the data on the matched groups are the most reliable, it is of interest to note the extent to which those for the entire group of 108 children are in agreement. For economy of space only the most pertinent data have

been summarized in table 8. The results entirely confirm those for the matched groups. By every method of comparison the children given a supplement show on the average a somewhat greater advance in osseous development during the year than do the children not given a supplement.

Taking the results of all comparisons, then, both for the 24 matched trios and for the entire group, it is clear that, regardless of the method of analysis used, the milk groups seem to have excelled in measurable degree the control children in their rate of osseous development, as indicated by the increase of ossification in the carpal bones. The differences tend consistently in the same direction, in favor of the milk groups. Although their superiority is not great, the differences are of such size that, associated with this consistency of direction, they justify the conclusion that they are significant and can reasonably be attributed to the dietary supplement. The differences between the milk groups were small, variable in direction and insignificant. These results are moreover in agreement with those for height and weight, which were reported in the preceding article.¹

COMMENT

Interpretation of the results of this study must be made with due consideration for the method used in assessing osseous growth. The question might be raised as to whether it is legitimate to use standards derived from the more favored socioeconomic group of the University of Chicago Laboratory Schools to assess the progress of children in an institution. The answer, according to Todd, would be "yes," because the standard represents a relatively stable group and therefore suitable for purposes of comparison. All dietary groups of the present study were retarded by more than 10 per cent, according to these standards. Even if it is assumed that, owing to heredity, this is a normal variable for these children, it is still a fair standard to use in comparing the progress of the three dietary groups, since the same standard is applied to all and since it is relative rather than actual gain that is important. It seems probable, however, that the Carter norms represent more nearly standards which should be attained on the average by well nourished children and that the negative deviations of the children of this study represent nutritional retardation. This is indicated by the fact that the children receiving only 1 pint (473 cc.) of milk supplement decreased their deficits in ossification ratios by an amount equivalent to approximately one third of a year's growth.

Most writers on this subject of anatomic age have appeared to ignore the nutritional factor save as it is accounted for in socioeconomic status. Todd,¹³ however, described four markedly different series of norms

13. Todd, T. W.: Human Bodies and Human Beings, *Sigma Xi Quart.* **21**:123, 1933.

which he obtained from (1) bodies of children who had died of various causes, (2) children in a low economic group, (3) average public school children and (4) winners in a school health contest; he indicated that the differences may be in part attributed to nutrition. The present study is the first to demonstrate experimentally by this method the effect nutrition may have on rate of osseous development in children from 4 to 15 years of age.

The lack of any significant difference between the group receiving plain evaporated milk and the group receiving irradiated evaporated milk may have several explanations. In the first place, the children may have been previously obtaining enough vitamin D for their needs. The home was in the country, and the children were out of doors most of their waking hours from early spring till late fall. They may therefore have obtained sufficient vitamin D from sunshine, enough being stored to last them through the winter months. A second explanation is that the 70 units of vitamin D which the milk supplied may not have been enough to produce measurable differences under the conditions of the experiment, even though it may have had a favorable influence. Even though the groups were as well matched and all other conditions were as well controlled as possible in an experiment of this type, variables were bound to occur, which might obscure small differences due to experimental procedure. Furthermore, several other dietary constituents were supplied in much more abundant amounts by the supplement than vitamin D, notably calcium, phosphorus and vitamins A, B₁ and B₂, and some or all of these were apparently limiting factors for the growth of bone, as judged by the favorable effect of milk alone. It may be, then, that vitamin D was also needed but that larger amounts would be required to demonstrate this fact.

Of particular interest in connection with these results is the difference which the simple addition of a pint of milk made in the growth of these children. The regular institutional diet lacked a number of dietary essentials, and the milk supplied some of these. There is probably no other single addition that would have added as much in quality with a similar addition of energy value. Although the diet was not thereby made perfect, the daily addition of the constituents of a pint of milk made a considerable difference in the skeletal development in this group of children. A third of a year's growth is an appreciable amount of gain over the average to be expected from one simple addition. Even with this supplement, however, the diet was still far from optimum, especially in vitamin C. It would be of interest to know how much of their arrears in osseous development these children might have made up in a year had a fully adequate diet been provided and how nearly they would approach the standards if this optimum diet or even the milk supplement could be continued throughout the period of growth.

SUMMARY

Roentgenograms of the wrists and hands of 108 children were taken at the beginning and at the end of a calendar year, and the progress in osseous development, as indicated by changes in the Carter ossification ratio, was followed. One third of the children were kept on the institutional diet as controls; one-third were given a pint equivalent of evaporated milk, and one-third were given an equal amount of irradiated evaporated milk. The most significant comparisons are those made for 24 selected trios of children, including 1 child from each dietary group, who were matched at the beginning for sex and for stage of osseous development.

By all methods of comparison the groups given a supplement showed somewhat greater progress than did the control group; these differences all tended in the same direction and were significant. There was no significant difference between the two groups receiving milk. Though all groups at the outset were retarded in respect to the Carter norms and were still retarded at the end of the study, both the groups given a supplement reduced their deficits to a greater degree than did the control group. This is shown by the following summary:

1. The percentage of children in more favorable relation to the Carter standard for age at the end than at the beginning of the study was 17 for the control, 50 for the milk and 46 for the D milk group.
2. The mean gain in Carter points for the three groups was 6 for the control, 8.3 for the milk and 8.2 for the D milk group, an advantage of 2.3 and 2.2 points, respectively, in favor of the milk groups.
3. The control group as a whole gained 79 per cent of the expected quota; each group given a supplement gained 115 per cent of the expected amount.
4. In the matched trios the control child made the greatest annual gain in 5 (21 per cent) of the comparisons, the child given plain milk in 10½ (44 per cent) and the child given D milk in 8½ (35 per cent). The amount of the superiority is shown in a comparison of the partners in the groups as to differences in variation from expected gain, the most accurate test of the data. The mean advantage of the children in the groups receiving milk over their control partners was 2.7 points. This difference is statistically significant. In terms of growth it amounts to more than a third of a year's quota of expected gain.
5. The daily addition of the constituents of a pint of milk proved a factor of safety in a rather mediocre institutional diet.

Grateful acknowledgment is made to Prof. Frank N. Freeman, of the Department of Education, who made available facilities for studying the roentgenograms, and to Dr. Charles D. Flory and Dr. E. C. Bolmeier, of the same department, for their generous help and criticism. Thanks are also due the Ritter Dental Equipment Company, especially Mr. J. M. Dickinson, for the loan of the x-ray apparatus.

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EFFECT OF A DIETARY SUPPLEMENT ON OSSIFICATION OF THE BONES OF THE WRIST IN INSTITUTIONAL CHILDREN

II. EFFECT OF A COD LIVER OIL SUPPLEMENT

VERA MACNAIR, PH.D.

ROCK HILL, S. C.

This investigation is one of a series undertaken to determine the response of bone growth in children to an improvement in nutrition. Ossification in the bones of the wrist has been the criterion of bone development; several food supplements have been used to improve nutrition. The effect of the daily addition to an institutional diet of a pint (473 cc.) of milk, plain or irradiated, was described in a previous article.¹ The present report concerns the effect of another supplement, cod liver oil.

The plan in the several studies was to find out under experimental conditions whether the rate of ossification would be modified by a dietary supplement in a group of children who were considered an average sample and who were receiving average diets. The striking effect of some specific supplements in cases of obvious deficiency diseases, such as rickets, is well known. As quality of bone may be an indication of previous nutritional history, a definite change in rate of ossification might be expected in response to improved nutrition even when to all outward appearance there had been no change.

In the earlier study milk was an appropriate addition to a diet which had previously averaged between a cup and a pint of milk per child daily and which was correspondingly poor in other protective foods. The children in the study were divided into three comparable groups, one continuing to receive the institutional diet, one receiving an additional pint of reconstituted evaporated milk and one an additional pint of irradiated evaporated milk per child per day. One of the somewhat unexpected results was that, while the groups given milk made signifi-

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This paper is numbered "II" because it is the second in a series of studies on ossification. The first paper in this series is that cited in footnote 1 (which was paper II of a series of studies of the physical status of a group of children).

1. MacNair, V., and Roberts, L. J.: Effect of a Milk Supplement on the Physical Status of Institutional Children: II. Ossification of the Bones of the Wrist, *Am. J. Dis. Child.* **56**:494 (Sept.) 1938.

cantly better gains in ossification than the control group, there was no appreciable difference between the advance made by those who had plain milk and those who had irradiated milk. One of several possible reasons for this may have been that the additional pint of irradiated milk added but 70 units of vitamin D a day. The effect of the other milk constituents, for which there was great need, may have obscured the effect of the vitamin. The question naturally arose as to what effect vitamin D might have on rate of growth in normal bone if given in such a way as to make possible more specific measurement of its effects.

Cod liver oil was a logical supplement to the diet in the second study for several reasons. First, it emphasized the addition of vitamin D. The daily dessert spoonful of cod liver oil which was given each child contributed approximately ten times the amount of this vitamin contained in the pint of irradiated milk. It also increased the vitamin A three or more times. Second, the regular diet of the homes chosen for the study on cod liver oil, while it was not perfect, was much better than that of the first institution. Milk was a substantial part of the diet, while fruits and vegetables were served the year around. The added cod liver oil, then, was somewhat more specific in this case than the milk which supplied many essentials deficient in the previous diet. Cod liver oil was also an appropriate supplement in the Chicago area, which is thoroughly blanketed from the potent rays of the sun for a considerable part of the year. The homes of the children of this study were within the confines of the city. The study on milk was done in a home outside Chicago, where the air is comparatively clear.

That there is a relation of nutrition to quality and growth of bone is well known. In cases of extreme deficiency, such as rickets, in which diet alone may remedy the defective calcification and change in quality may be watched by roentgen study, there is some difference of opinion as to the effect on rate of development. Most investigators have stated the belief that the rate is more or less decreased by rickets, the change depending on the severity and duration of the disease. With children the problem is complicated by the fact that a deficiency causing rickets is likely to be accompanied by other deficiencies, which may influence growth. The condition not so extreme as to show outwardly or to be classed with the deficiency diseases but manifesting the type of difference in quality and growth of bone with which this study is concerned was described by Sherman:²

. . . growing children whose height, weight and appearance are normal, may have a calcium-poor condition of body which even the best physical examination

2. Sherman, H. C.: *Chemistry of Food and Nutrition*, ed. 5, New York, The Macmillan Company, 1937.

cannot reveal, but which is revealed by the chemical evidence of the calcium balance experiments determined directly upon children of different ages and fully confirmed by analyses of the bodies of experimental animals.

Is there in these cases, accompanying the calcium-poor condition, a corresponding change in rate of bony development? In this less extreme condition will the rate of ossification parallel the quality of bone which has been determined by the nutritional history, or will it continue at a nearly normal rate, as might be expected from the work of Jackson and Stewart³ and others on rats, Aron on dogs⁴ and Waters⁵ on calves? These workers found that when a deficient diet was fed which just allowed the weight to be maintained, growth in length of the skeleton continued for some time at the expense of first the fatty tissue and then the muscles. Cammerer,⁶ Morgulis⁷ and others reported a similar kind of growth in malnourished young children, that is, increase in length with accompanying slenderness of form and poor muscular development. If in cases like these the skeleton continues to grow for a time, it could be expected to maintain a nearly normal rate under much less serious conditions.

Nutrition could be expected to affect rate of ossification as well as quality. The effect of socioeconomic status, which has been studied and discussed by Stettner,⁸ Todd⁹ and others, carries an implication of nutritional factors. Stettner, studying development of German children by means of roentgenograms of the hand, reported a difference in the quantity and quality of ossification in children of laborers, rural children and urban children of the middle class, the last having the best quality and highest rate of osseous growth. He suggested that hygienic conditions should be studied in connection with these differ-

3. Jackson, C. M., and Stewart, C. A.: Effect of Underfeeding and Refeeding upon the Growth of Various Systems in the Body, *J. Exper. Zoöl.* **30**:97, 1920.

4. Aron, H.: Nutrition and Growth, *Philippine J. Sc. (Sect. B)* **6**:1, 1911.

5. Waters, H. J.: The Capacity of Animals to Grow Under Adverse Conditions, *Proc. Soc. Promotion Agric. Sc.* **29**:3, 1908; **30**:70, 1909.

6. Cammerer, W.: Untersuchungen über Massenwachstum und Langerwachstum der Kinder, *Jahrb. f. Kinderh.* **36**:249, 1893.

7. Morgulis, S.: Fasting and Undernutrition, New York, E. P. Dutton & Company, 1923, pp. 289-308.

8. Stettner, E.: Ueber die Beziehungen der Ossification des Handskeletts zu Alter und Längenwachstum bei gesunden und kranken Kindern von der Geburt bis zur Pubertät, *Arch. f. Kinderh.* **68**:342 and 439, 1920; **69**:27, 1921; **70**:69, 1922; Ossificationsstudien am Handskelet: III. Die "physiologische Osteoporose," *Ztschr. f. Kinderh.* **52**:1, 1932.

9. Todd, T. W.: Roentgenographic Appraisalment of Developmental Growth in the Skeleton, in *Growth and Development of the Child*: IV. Appraisalment of the Child, White House Conference on Child Health and Protection, New York, Century Company, 1932, pp. 258-285.

ences. Wallis¹⁰ found evidence that in three groups of young children with almost identical economic background and diverse European origin the amount of growth was the same, which indicated that the factors in the socioeconomic status in these cases were more potent than heredity in determining rate. Todd¹¹ stated the opinion that nutrition may explain, in part at least, the different norms for osseous development that he found in four classes of children. The most advanced were those of children who won a school health contest; in decreasing order followed the norms for average school children of Cleveland, children of low economic status and children who had died from causes other than accident.

Other tendencies of growth relevant to the present study have been noted. Baldwin¹² stated that between 6 and 17 years of age children under poor nutritional conditions grow as fast or faster than well nourished children, but before that time they are shorter and hence never attain to equal height. Moreover, according to Flory,¹³ there appears to be a tendency at the time of puberty for bone to mature and for the area of the wrist to more or less fill with bones articulated as in the adult, whatever the previous lag. This does not mean that there may not be a continuing lag due to external causes; but there seems to be a tendency to mature with the materials at hand, whatever they are. This, of course, correlates with the evidence that less well nourished people are of smaller adult stature.

The retarding effect of illness, especially fevers, on rate of bony development has been noted by several authors, with a suggestion that it may be through disturbance of nutritional processes that the retardation is effected. Pryor¹⁴ stated that "conditions of health, accidents, disease, anything that would interfere with the blood supply or modify metabolism would be likely to delay or modify the process of ossification." Rotch¹⁵ also stated that epiphysial development can be affected only by normal or abnormal changes in metabolism. Todd⁹ listed such disorders as diarrhea, measles, whooping cough and mumps as likely

10. Wallis, R. S.: *How Children Grow*, Studies in Child Welfare, Iowa City, University of Iowa, 1931.

11. Todd, T. W.: *Human Bodies and Human Beings*, Sigma Xi Quart. **21**: 123, 1933.

12. Baldwin, B. T.: *Physical Growth and School Progress*, Bulletin 10, United States Department of the Interior, Bureau of Education, 1914.

13. Flory, C. D.: *Osseous Development in the Hand as an Index of Skeletal Development*, Monographs of the Society for Research in Child Development, National Research Council, 1936, vol. 1, no. 30.

14. Pryor, J. W.: *Some Observations on the Ossification of Bones in the Hand*, Bull. Univ. Kentucky (no. 11) **8**:1, 1916.

15. Rotch, T. M.: *Roentgen Ray Methods Applied to the Grading of Early Life*, Am. Phys. Educ. Rev. **15**:396, 1910.

to cause delay in the appearance of the carpal centers and indicated a possible relation of the delay to disturbance of the nutritional condition by the disease.

The close interrelation of the factors which may affect metabolism or nutrition and therefore development of bone, in the opinion of workers who have studied this phase of growth, is shown by the observation of Wallis¹⁰ on a group of children whose growth, anthropometric and osseous, she followed for several years. She said of them:

. . . these children belong to a favored class whose economic environment offers the possibility of attaining the maximum growth inherent in their family lines. . . . Very few do not receive optimum diet throughout the year. . . . Careful school health programs have greatly reduced the spread of contagious diseases which result in retardation of growth.

Flory found that recent norms for the Carter ossification ratio obtained from children of the University of Chicago Laboratory School were higher than those obtained from the same group thirteen to fifteen years ago. He suggested the explanation that in the last decade nutritional management in this group has been significantly improved with a wholesome effect on the osseous growth of the subjects, which affected the average for their age. Again, in discussing some of the studies of ossification which have been made, Flory said that if retardation can occur only when disease is present, then in some children there must be hidden disorders which are not detected by the ordinary medical examination. And later he stated that "the nutritional aspect of the problem needs further investigation."

There have been very few studies of the relation of calcium and vitamin D to growth in human beings in whom various aspects of growth, including skeletal, were followed quantitatively. Daniels, Hutton, Stearns and Hejinian,¹⁶ studying the relation of the rate of growth in infants to diet from the standpoint of physical measurements and nitrogen metabolism, found that children receiving cod liver oil grew at a more rapid rate than children given the same diet without cod liver oil. The physical measurements included growth in length, which is one aspect of skeletal growth. Jeans, Stearns and their co-workers studied a series of infants throughout the major portion of infancy (as reported by Jeans¹⁷). They obtained comprehensive data on intakes of milk and vitamin D, calcium and phosphorus retention, levels of

16. Daniels, A. L.; Hutton, M. K.; Stearns, G., and Hejinian, L. M.: The Relation of Rate of Growth in Infants to Diet, *Am. J. Dis. Child.* **37**:1177 (June) 1929.

17. Jeans, P. C.: Vitamin D Milk: The Relative Value of Different Varieties of Vitamin D Milk for Infants; a Critical Interpretative Review, *J. A. M. A.* **106**:2066 (June 13); 2150 (June 20) 1936.

calcium and phosphorus in the serum, linear growth and increases in weight, dentition, motor achievement, and ossification as shown by a series of roentgenograms of a wrist of each infant. There were three divisions: groups 1 and 2 received whole acidified fresh and evaporated milk, respectively, and 340 units of vitamin D daily, with orange juice and sieved vegetables and fruits; group 3 received the same foods but only 60 to 135 units of vitamin D a day. The results of the study were given by Jeans:

The serum calcium and phosphorus values in all three groups were normal. . . . Each infant in groups 1 and 2 grew both in length and in weight at greater than the average rate; dentition was early, most of the infants having cut two teeth by 6 months of age and six teeth by 9 months of age. No infant attained the age of 8 months without having cut at least two teeth. Carpal centers became visible to the X-rays more rapidly than usual. The infants were physically very active. The majority were able to sit unsupported by 6 months of age and could pull themselves to standing by 9 months. In short, the infants of these two groups were superb physical specimens. The retentions of calcium, phosphorus and nitrogen were very high, indicating that, notwithstanding the rapid growth, the mineralization of bones and the muscular development were above the average.

The rate of growth of the infants of group 3 was much slower than that of the babies in the other two groups, although it could be considered "average." Dentition was late; most of the infants did not begin cutting teeth until 8 or more months of age. None of these infants were able to sit unsupported at 9 months of age; two were able to do so by 10 months, but the muscles were flaccid and the posture poor. The retentions of calcium and phosphorus by the babies of this third group was much less than in the babies of groups 1 and 2; so much less that the slower rate of growth did not compensate, and the retention per kilogram of weight increase and per centimeter of growth in length was definitely lower than the retention for the babies of groups 1 and 2.

This work is of particular interest here, first, because in it the effect of diet on skeletal development was studied by relating linear growth and the appearance of the carpals to a dietary constituent under consideration in this study; second, because the two groups of children, not suffering from obvious deficiency disease but differing in quality of growth, were similar to the groups of children with which we are concerned in the present series of studies.

A few investigators, then, have reported studies which suggest in varying degrees and several ways that nutritional status must be included among the influences governing quantity as well as quality of osseous growth.

The purpose of this series of studies, as indicated earlier, was to observe under conditions carefully controlled the effect of nutritional status on the rate of bone growth and to determine its magnitude as shown by measurement of the advance in ossification in the carpal area.

METHODS

The subjects of this study lived in several homes for children in Chicago and were between the ages of 2.5 and 10.5 years. This age range was chosen for several reasons. Before adolescence bone development is more rapid, and individuals vary less, than during adolescence. In addition, "as the child grows older, he becomes far less susceptible than in early life to the effect of those influences that disrupt skeletal maturity."⁹ Then, too, the Carter ossification ratio used in these studies to assess skeletal development gives a better picture during preadolescent ages than during the teen ages (Flory¹³). Therefore the decision was made to use preadolescent children for the study on cod liver oil. Administration of cod liver oil to one of two matched groups of children was started early in March 1935. The groups were formed of partners in matched pairs, which were chosen after study of 117 roentgenograms, 56 of boys and 61 of girls, taken in February. By means of these initial roentgenograms, 52 pairs of children were matched for sex, skeletal maturity and chronologic age. There were 24 pairs of boys and 28 of girls. One of each pair received the institutional diet with no addition, and the other received a daily dessertspoonful of cod liver oil besides the regular diet. This amount of cod liver oil added approximately 700 units of vitamin D and 4,500 units of vitamin A.

In the year this study was made, February 1935 to March 1936, the usual turnover in such homes was exceeded, as it was a year of recovery and children were returning to reestablished homes. Therefore by the end of the year many pairs had lost a partner. There remained at the end 83 of the original 117 children. Fifteen of these, 6 control and 9 experimental girls living in a small home, were dropped because there had been changes which made the groups hardly comparable. In the second home no well matched partners were left, but the control and the experimental group, consisting of 7 and 8 children, respectively, were still comparable. In a larger home there remained 53 children, including 19 pairs matched for initial skeletal development. The data obtained from the 19 pairs will be presented in some detail.

The home in which the 19 pairs lived is one of the best of its kind. The dietitian in charge of the food supply is interested in the growth of the children and keeps monthly records of weight. Before and during the study each child received two half-pint bottles of milk per day in the summer and three during the winter months, in addition to the milk used in cooking. The intention of the management of the institution is that every child shall average a quart of milk per day. Fruits and vegetables are a regular part of the diet. A graduate nurse has charge of the dispensary and of the well equipped infirmary, and there is a regularly attending physician. Varied backgrounds are represented among the children, who are of foreign or American ancestry and of poor or middle class families; usually the parents have separated, or only one is left to support the child. Very few of the children are orphans.

The graduate nurse was responsible for the administration of the cod liver oil. To a number of the children living in the main building she herself gave the daily dessertspoonful. When matrons in the cottages administered the oil, she supplied them with the oil and through frequent contact supervised the dosage and the keeping of records. In the infirmary records were kept of illnesses, medicines or special diets given and of absences at city hospitals. A record of the administration of cod liver oil was added for the period of the study. The policy was to disturb the regular routine of the institution as little as possible. The

person in charge of the project (V. M.) was in constant personal contact with the staff and home, taking the monthly weights with the dietitian and having frequent conferences with the nurse and superintendent.

The development of bone in the wrist was followed by means of roentgenograms of the right hand and forearm. The method of taking and measuring the roentgenograms has been described in some detail in a previous report.¹ The essentials will be reviewed briefly here. When the roentgenograms were taken, special care was exercised to have them uniform in regard to position of wrist and distance from the target. The exposure was adjusted as accurately as possible to the size and development of the hand in order that the films might have comparable density. The area of the wrist was chosen for study because (1) ossification in the hand and forearm has been shown to be representative of that in other parts of the skeleton, (2) uniform roentgenograms of this area are comparatively easy to obtain, and (3) the most comprehensive norms of skeletal development available are based on measurement of these centers.

Two methods of assessing bone development were used, as in the previous study. The first, a qualitative method (which includes quantitative aspects) employing the Flory inspectional age scale, matched children for development

TABLE 1.—*Initial Mean Carter Indexes and Chronologic Ages of the Control and the Experimental Group Previously Matched as to Development Toward Maturity*

Group	Carter Index, Ossification Ratio		Chronologic Age, Years	
	Boys	Girls	Boys	Girls
Control.....	36.8	59.5	6.2	7.3
Experimental.....	38.3	57.8	6.4	7.5

toward the mature form.¹⁸ The second, a quantitative method utilizing the Carter ossification ratio, was used to determine and to compare increments of growth objectively.¹⁸ This ratio, or index, relates the sum of the areas of the roentgen shadows of the carpal bones and the epiphyses of the radius and the ulna to the area of the wrist, i. e., the area ossified to the area to be ossified:

$$\frac{\text{Sum of areas of carpal bones}}{\text{Area of carpal quadrilateral}} = \text{Carter index, or ossification ratio.}$$

The areas are obtained by circumscribing with a planimeter the shadows of the carpal bones and also the outline of a designated quadrilateral which represents the wrist.

As soon as the initial roentgenograms were measured according to the Carter technic, the partners as tentatively set up by the Flory skeletal age were rechecked by the Carter ossification ratio with the intention of making any shifts necessary for matching them on this basis as well. No shifts were found necessary, however. This might be expected in view of the fact that the ossification ratio and the inspectional age have been shown by Flory to correlate, the respective figures for boys and girls being 0.833 ± 0.024 and 0.884 ± 0.023 for these ages. The small differences between partners balanced each other, and the means for the two groups are therefore fairly close, as is shown in table 1. The mean Carter indexes for

18. Freeman, F. N., and Carter, T. M.: A New Measurement of the Development of the Carpal Bones and Its Relation to Physical and Mental Development, *J. Educ. Psychol.* **15**:257, 1924.

children in the control and the experimental group are 36.8 and 38.3 for boys and 59.5 and 57.8 for girls, respectively. Mean chronologic ages are similarly close, being 6.3 and 6.4 years for boys and 7.3 and 7.5 for girls in the control and the experimental group, respectively.

RESULTS

Before the data from this study are presented, it is appropriate to consider what might be expected as a result of adding cod liver oil to the diet of these children. It was mentioned earlier that protective foods were well represented in the institutional diet. Milk, vegetables and fruits were served regularly. The total amount of food seemed liberal. Therefore it is highly improbable that any nutritional essential was entirely lacking, though it is possible that one or more, including vitamin A or vitamin D, might have been present in less than optimum amounts. Both vitamin A and vitamin D are concerned in the process of ossification. Deficiency in vitamin D is characterized by failure of osteoid tissue to lay down or to hold calcium salts. In complete vitamin A deficiency in rats epiphyseal activity and bone growth cease, growth being resumed on restoration of vitamin A to the diet.^{18a} The Mellanbys¹⁹ also showed the relation of this vitamin to teeth and related structures. The response of the children receiving cod liver oil would depend primarily, then, other factors being constant, on whether vitamins A and D had previously been supplied to them in optimal amounts. If either or both of these vitamins had been present in less than optimal amounts, an improvement in nutrition and a consequent increase in rate of bone growth might be expected as a result of the cod liver oil supplement, which added approximately 700 units of vitamin D and 4,500 of vitamin A. If both had been adequate, no difference between the two groups could be expected.

What are the results? When the data from the initial roentgenograms had been collected, it was apparent that nearly half the children were above and somewhat more than half were below the Carter norms for their age; a third were 10 per cent or more below. It should be noted here that the Carter norms were obtained from children of the University of Chicago Laboratory School, a favored socioeconomic group. Therefore it is probable that they represent what is desirable

18a. Hess, A. F.; McCann, G. F., and Pappenheimer, A. M.: Experimental Rickets in Rats, *J. Biol. Chem.* **47**:395, 1921. Wolbach, S. B., and Howe, P. R.: Vitamin A Deficiency, in *Growth and Development of the Child: III. Nutrition*, White House Conference on Child Health and Protection, New York, Century Company, 1932, pp. 178-180. Dawson, A. B.: A Historical Study of the Persisting Cartilage Plates in Retarded or Lapsed Epiphyseal Union in the Albino Rat, *Anat. Rec.* **43**:109, 1929.

19. Mellanby, E.: *Nutrition and Disease: The Interaction of Clinical and Experimental Work*, Edinburgh, Oliver & Boyd, 1934.

TABLE 2.—Deviation from Carter Index for Age for All Children at Beginning and End of Study, with Changes During the Year in Relation to Mean Index for Age and Sex and in Relation to Expected Gains

Pair No.	Subject	Sex	Carter Index Beginning	Mean Index Age	Deviation at Beginning		Carter Index End	Mean Index for Age	Deviation at End		Change in Deviation from Mean for Age		Gain in Score for Year		Per-centage of Expected Gain
					Points	Percentage			Points	Percentage	Points	Percentage	Actual	Expected	
19 Matched Children of Control Group															
1	G. B.	F	65	60	+ 5	+ 8	74	71	+ 3	+ 4	- 2	- 4	9	11	82
2	M. L. B.	F	32	37	- 5	- 14	42	46	- 4	- 9	+ 1	+ 5	10	9	111
3	H. C.	F	65	71	- 6	- 9	79	81	- 3	- 4	+ 3	+ 5	13	10	130
4	N. O.	F	71	64	+ 7	+ 11	81	76	+ 5	+ 7	- 2	- 4	10	12	83
5	V. L. C.	F	44	41	+ 3	+ 7	52	51	+ 1	+ 2	- 2	- 5	8	10	80
6	D. F.	F	74	74	0	0	75	84	- 9	- 11	- 9	- 11	1	10	10
7	D. I.	F	76	70	+ 6	+ 9	83	81	+ 2	+ 3	- 4	- 6	7	11	64
8	M. B. L.	F	34	34	- 12	- 26	43	53	- 12	- 22	0	0	9	9	100
9	V. S.	F	81	46	+ 2	+ 3	87	88	- 1	- 1	- 3	- 4	6	9	67
10	L. F.	F	55	49	+ 6	+ 12	67	58	+ 9	+ 16	+ 3	+ 4	12	9	133
11	C. C.	M	39	47	- 8	- 17	47	56	- 9	- 11	- 1	+ 1	8	8	89
12	A. C.	M	34	39	- 5	- 13	42	47	- 5	- 9	+ 1	+ 2	10	9	111
13	R. D.	M	40	50	- 8	- 18	56	59	- 3	- 5	+ 1	+ 3	2	9	92
14	J. L.	M	54	46	+ 8	+ 17	60	56	+ 4	+ 2	+ 1	+ 1	113	8	113
15	H. L.	M	51	45	+ 3	+ 6	44	43	+ 1	+ 2	+ 1	- 4	8	9	89
16	N. P.	M	36	34	+ 2	+ 6	38	39	+ 1	+ 1	- 0	- 0	100	7	100
17	R. P.	M	31	32	- 1	- 3	33	39	- 4	- 13	+ 1	+ 10	7	7	117
18	C. R.	M	15	20	- 5	- 25	22	26	- 4	- 15	+ 1	+ 0	4	6	50
19	B. T.	M	25	39	- 14	- 36	29	47	- 18	- 38	- 4	- 2	4	8	50
Total			1,011		18			1,119	- 43		- 25	- 20	148	173	1,651
Average					1.78				- 3.84				7.8	9.1	86.9
Percentage of expected gain for group..... 85.6															
Children of Additional Control Group															
20	S. A.	M	54	51	+ 3	+ 6	63	59	+ 4	+ 7	+ 1	+ 1	9	8	113
21	D. B.	M	48	53	- 5	- 10	59	62	- 3	- 5	+ 2	+ 5	11	9	122
22	J. L.	M	72	66	+ 6	+ 9	79	74	+ 5	+ 1	+ 5	+ 8	8	8	88
23	V. H.	F	26	24	+ 2	+ 8	29	31	- 2	- 7	- 4	- 15	3	7	43
Total			1,205		- 42			1,345	- 43		- 31	- 37	174	205	1,967
Average					- 0.91				- 3.20				7.6	8.9	85.5
Percentage of expected gain for group..... 84.9															

19 Matched Children of Experimental Group

1	Ma. W.	F	59	71	-12	-17	73	81	-8	-10	+4	+7	14	10	140
2	N. A.	F	33	35	-2	-6	44	45	-1	-2	+1	+4	11	10	110
3	F. T.	F	63	78	-15	-19	76	87	-11	-13	+1	+6	13	9	144
4	D. R.	F	73	63	+10	+16	80	74	+6	+8	-	-8	7	11	64
5	D. J. D.	F	37	53	-16	-30	46	62	-16	-26	0	+4	9	9	100
6	D. S.	F	74	61	+13	+21	84	71	+13	+19	0	+2	10	10	100
7	J. T.	F	76	81	-5	-6	83	89	-6	-7	-	-1	7	8	88
8	B. M.	F	82	45	-12	-27	43	53	-10	-19	+2	+8	10	8	125
9	V. W.	F	48	80	+2	+3	88	89	-1	-1	-3	+4	6	9	67
10	D. M. S.	F	43	63	+5	+12	55	52	+3	+6	-2	-6	7	9	78
11	B. O.	M	39	63	-24	-38	50	71	-21	-30	+3	+8	11	8	138
12	W. W.	M	36	37	-1	-3	44	46	-2	-4	-	-1	8	9	89
13	L. P.	M	49	44	+5	+11	61	52	+9	+17	+4	+6	12	8	150
14	L. D.	M	58	53	+5	+10	66	62	+4	+7	-	-3	8	9	89
15	F. W. B.	M	40	44	-4	-9	46	52	-6	-12	-2	-3	6	8	75
16	J. L.	M	43	39	+4	+10	51	47	+4	+9	0	-1	8	8	100
17	B. H.	M	34	30	+4	+13	41	36	+5	+14	+1	+1	7	6	117
18	C. B.	M	20	25	-5	-20	22	29	-7	-24	-2	-4	2	4	50
19	M. W.	M	26	29	-8	-10	33	33	0	0	+3	+10	7	4	175
Total			974		-51		1,131		-45		+6	+25	163	157	1,959
Average					-5.24					-3.98			8.6	8.3	105.2

103.8

Percentage of expected gain for group

Additional Children of Experimental Group

20	Jo. T.	M	15	19	-4	-21	18	24	-6	-25	-2	-4	3	5	60
21	L. A.	M	28	29	-1	-3	34	35	-1	-3	0	0	6	6	100
22	J. MeP.	M	29	31	-2	-7	33	37	-4	-11	-2	+7	4	6	67
23	J. M.	M	7	19	-12	-63	11	25	-14	-56	-2	+4	4	6	67
24	Ja. T.	M	18	26	-8	-31	21	31	-10	-32	-2	-1	3	5	60
25	R. W.	M	23	21	+2	+10	29	26	+8	+12	+1	+2	6	5	120
26	Gr. B.	F	84	80	+4	+5	93	89	+4	+5	0	0	9	9	100
27	E. C.	F	86	81	+5	+6	90	90	0	0	-5	-6	4	4	44
28	A. H.	F	46	49	-3	-6	33	58	-5	-9	-2	-3	7	9	78
29	E. R.	F	58	58	0	0	73	68	+5	+7	+5	+7	15	10	150
Total			1,387		-70		1,614		-78		-3	+23	224	227	2,845
Average					-5.05					-4.52			7.7	7.8	101.6

97.8

Percentage of expected gain for group

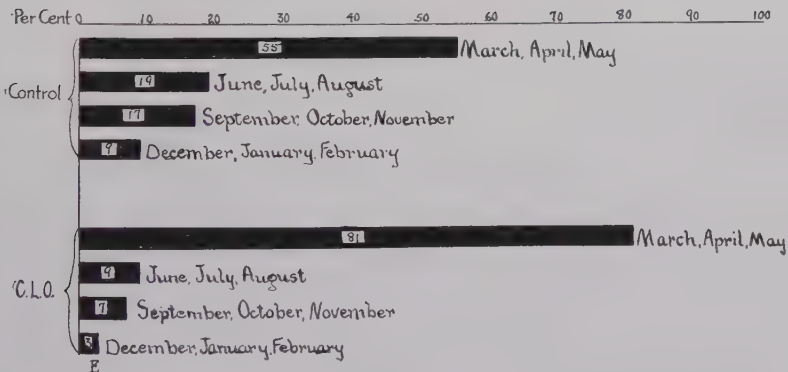
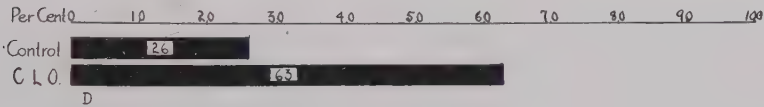
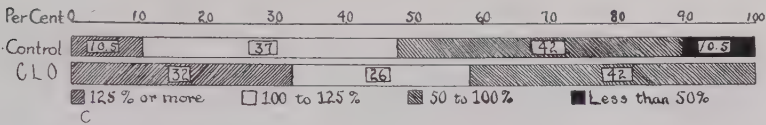
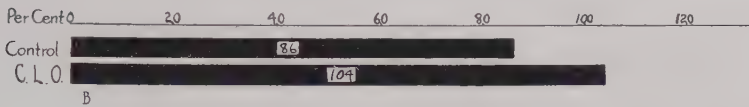
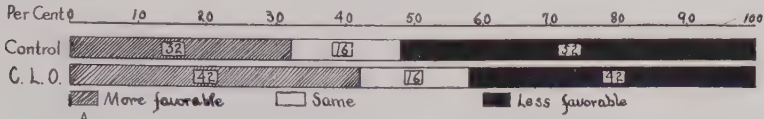
for all children rather than the actual average for all children or the average for those of the study. They are valuable as a means of comparison, however, because they have been obtained from a large number of children, 3,113, in a fairly stable group. With these norms as a basis of reference, the children of the study can be compared as to the relative amount of bone growth and the yearly gain in ossification. The relative status of each child, i. e., his deviation from the mean for his age, at the beginning and at the end of the study, was determined by comparing his initial and final ossification ratios with the Carter norms for his initial and final ages (table 2). The children whose ratios were 10 per cent or more below the means for their age would undoubtedly have been adjudged retarded by any standard taken from large numbers of average children. In both groups there were children who at the end of the year were still much below the average (table 3). In the control group the number retarded increased somewhat, from 47.5 to 57.5 per cent; in the group given cod liver oil the number retarded remained nearly the same, but here there was a slight shift of retarded children into a position of less retardation.

This change is shown more clearly by a consideration of the proportion of children in each group who improved their status or who lost in relation to the means for their ages. A child retarded at the beginning might still be retarded at the end of the year and yet might have made up a considerable amount of his deficit (table 4 and chart *A*). Of the control group 32 per cent, as compared with 42 per cent of the children given cod liver oil, were in a more favorable relation to the mean at the end of the year than at the beginning, while 52 per cent were in a less favorable relation, as compared with 42 per cent of the children given cod liver oil.

There are, however, more exact methods of showing differences in the year's growth of bone between the children who received the supplement and those who did not. These include three kinds of comparison: (1) of the matched groups, the control group and that taking cod liver oil, as wholes; (2) of proportions of the group in which advances of various sorts were made, and (3) of matched partners. The results are shown in table 2 and in the summaries given in tables 4 to 6.

In comparing the matched groups as samples of (1) children 3 to 10 years old receiving the institutional diet and (2) children of the same age receiving cod liver oil in addition, the pertinent figure is the percentage of the expected gain made by each group. In determining this figure the difference between the ossification ratio determined at the beginning and that noted at the end of the year represents a child's actual gain, and the difference between the norms for his initial and his final age represents the gain which might be expected of him. From these two values, the percentage relation of the actual gain to the expected gain can be computed for each child.

$$\frac{\text{Actual gain} \times 100}{\text{Expected gain}} = \text{Percentage of expected gain actually attained.}$$
 It is possible also to total both the actual and the expected gains for all children in each of the two groups and thus to determine similarly the percentage of expected gain made by control and experimental groups



A, percentage of children in each group in more and in less favorable relation to the Carter mean for their age at the end than at the beginning of the year. "C.L.O." indicates the group given cod liver oil. B, percentage of the expected gain made by each group. C, percentage of children in each group making the gains specified, in percentage of the expected gain. D, percentage of the 19 pairs in which the specified partner made the best gain. E, proportion of the year's illness in each group for the specified quarter of the year.

when each is considered as a unit. Considering first the latter method of analysis, one finds (table 2 and chart *B*) that the control group made but 86 per cent of its expected gain in bone growth while the group taking cod liver oil made 104 per cent of its expected quota.

TABLE 3.—*Percentage of Children in Matched Groups Having the Specified Relation to the Mean at the Beginning and at the End of the Experimental Year*

Status	Control				Experimental			
	Beginning		End		Beginning		End	
	No.	%	No.	%	No.	%	No.	%
Even with mean or above.....	10	52.5	8	42	8	42	8	42
10% or more.....	3		1		7		3	
5 to 10%.....	5		2		0		4	
0 to 5%.....	2		5		1		1	
Below mean, less than 10%.....	3	16	5	26	4	21	4	21
1 to -5%.....	1		3		1		3	
-5 to -10%.....	2		2		3		1	
Below mean, 10% or more.....	6	31.5	6	31.5	7	37	7	37
to -15%.....	2		2		1		3	
-15% or more.....	4		4		6		4	
Totals.....	19	100	19	100	19	100	19	100

TABLE 4.—*Percentage of Children in Each Matched Group in More and in Less Favorable Relation to the Mean for Age at the End Than at the Beginning of the Experimental Year*

Status	Control Group		Cod Liver Oil Group	
	No.	%	No.	%
In more favorable relation.....	6	32	8	42
In same relation.....	3	16	3	16
In less favorable relation.....	10	52	8	42

TABLE 5.—*Percentage of Matched Children Making Specified Percentage of Expected Gains for the Year by Dietary Groups*

Amount of Gain, % of Expected Gain	Control Group		Cod Liver Oil Group	
	No.	%	No.	%
100 or more.....	9	47.5	11	58
125 or more.....	2	10.5	6	32
100 to 124.....	7	37.0	5	26
Less than 100.....	10	52.5	8	42
50 to 99.....	8	42.0	8	42
Less than 50.....	2	10.5	0	0

An analysis of the percentage of the expected gain made by the subjects in the two groups shows in children given cod liver oil the same tendency to excel (table 5, chart *C*). It is observed that the percentage of children making 100 per cent or more of their expected gains was greater in the group given a supplement than in the control group (58 per cent

versus 47.5 per cent). Moreover, fewer children in the group given cod liver oil made gains at the lowest levels and more children made gains at high levels than in the control group. Two of the control children made less than half the amount, and only 2, or 10.5 per cent of the group, made more than 125 per cent of the amount to be expected for their age, while in the group given cod liver oil none made less than half the expected gain and 6, or 32 per cent, made 125 per cent or more of their expected quota.

The most important comparison is that of the partners in the 19 pairs of children who were matched according to their skeletal development at the beginning of the study. As pointed out earlier, if the partners show like or nearly like development toward the mature pattern as judged by inspectional age, actual growth of bone as determined by the Carter ratio, and chronologic age, it is likely that they are in the same phase of growth. Direct comparison of partners is therefore the severest test of differences due to experimental procedure.

TABLE 6.—*Number of Times in Nineteen Matched Pairs the Specified Partner Made the Best Gain and the Amount of Superiority*

Partner Making Best Gain	Number of Times	Percentage	Excess, Carter Points	
			Total	Average
Control.....	5	26	14	2.8
Both the same.....	2	11	..	..
Cod liver oil.....	12	63	45	3.75
Difference in favor of partners given cod liver oil.....	..	..	31	1.63

From this standpoint, then, which of the partners made the best gains? Since the children were fairly well matched at the outset, the 2 children in each pair may be considered as having had an even start. If all conditions had been kept constant during the year, it might be expected either that the children in each pair would gain the same amount or that the higher gains would be about evenly distributed between the control and the experimental partners. If, however, the cod liver oil had an accelerating effect on development of bone and if this was the only variable introduced, the child in each pair having the supplement would presumably make the greater gain. The results of this method of analysis are given in table 6 and in the chart (*D*). It is at once evident that the best gains were by no means shared equally by the two groups but were predominantly attained by the partners receiving the cod liver oil supplement. In 5 of the 19 pairs the control child had better growth than his partner, while in 12 the child given cod liver oil did better than his control partner; in 2 pairs the partners made the same gain; i. e., the control partner excelled in 26 per cent and the experimental partner in 63 per cent of the comparisons. The fact that

not every experimental child outdistanced his control partner is not surprising, for other variables—especially illness, variations in consumption of food and absences from the institution—obscured the results. The amount of the difference between the partners and its statistical significance are important. The mean mathematical difference between the partners in the 19 pairs is $+1.63 \pm 0.55$ in favor of the partner receiving cod liver oil. This difference divided by its probable error is 3. This indicates that the difference may be significant, and not due to chance. This comparison of partners is the most direct and significant comparison of the progress of the two groups which can be made.

Thus in various kinds of comparisons of matched groups and matched partners the children given cod liver oil showed superiority, not large in any case but probably significant in the comparison of matched part-

TABLE 7.—*Progress in Osseous Growth of the Sixty-Seven Children of the Study During the Experimental Year*

Item	Control	Cod Liver Oil
Number of children.....	30	37
Percentage of children even with mean or above:		
Beginning.....	53	38
End.....	40	38
Percentage of children in more favorable relation to mean by 5% or more.....	13	22
Percentage of children in less favorable relation to mean by 5% or more.....	30	14
Percentage of expected gain attained.....	81	96
Percentage of children making expected gain or more.....	40	46
Less than 50%.....	17	8
125% or more.....	7	22
150% or more.....	0	11

ners. However, neither their size nor their statistical significance makes these differences between experimental and control groups important so much as the fact that they are consistently in the same direction, in favor of the children receiving cod liver oil. Therefore it seems that they can reasonably be ascribed to the experimental procedure.

The data from the study of the matched partners have been emphasized because they constitute a more precise measure of the experimental differences than do those from the study of the larger groups, but the data on the entire group of 67 (30 control children and 37 children given cod liver oil) are of interest. These are summarized in table 7. The table shows that, as in the 19 matched pairs, the experimental children advanced somewhat more than the controls. The percentage of those even with or above the norm remained the same in the group given a supplement, while in the control group it decreased from 53 to 40; 22 per cent of the children who had cod liver oil were in a more favorable relation to the mean for their age, by 5 per cent or

more, as compared with 13 per cent of the control children. The control group as a unit gained 81 and the experimental 96 per cent of the expected gain. Moreover, 17 per cent of the control children gained less than half the amount to be expected, and none made really large gains; 8 and 11 per cent are the respective figures for the group who took cod liver oil. Briefly, the evidence from the larger groups confirms that from the matched groups.

In connection with the significance of these differences there are two contributing factors to consider. First, at the home where the 19 pairs lived it is the custom to give cod liver oil for a week or two to any child who has had fever or a more serious disease, such as measles, scarlet fever or pneumonia. Sometimes, instead of the cod liver oil, a preparation containing cod liver oil, vitamin B complex and iron may be given. This procedure was not changed because of the experimental work. In this way 8 of the control children received a supplement of this kind for a week or so, the duration of the addition being as little as a week in most cases and as much as twenty-nine days in 1 case. An equal number of the experimental group were given some addition; i. e., the preparation of cod liver oil, vitamin B complex and iron was substituted for plain cod liver oil for periods similar in length to those of additions in the control group. In 2 cases an iron preparation was added, and in 1 case a vitamin C preparation was given for a week and then daily orange juice with the cod liver oil for a time.

Another custom of this home, as of most institutions of this sort, is to send children with any of the more serious contagious diseases to one of the Chicago hospitals equipped to take care of such patients. As a result, some of the children were away a month or more, and during their stay at the hospital the administration of cod liver oil was discontinued. Eight of the children who were taking cod liver oil had interruptions of this sort, and so the periods for the administration of the oil varied instead of being a full year for each experimental child as originally intended.

Second, among the variables which can be isolated and examined to some purpose are the duration and the severity of illnesses. Immediately after the first roentgenograms had been taken and the children had been divided into two groups which were matched as to skeletal maturity, there was an epidemic of children's diseases. In 1935 these diseases were rather more prevalent over the country than usual. Even among this comparatively well cared for group there were scarlet fever, measles, whooping cough, diphtheria (several cases) and pneumonia (several cases). As chance would have it, the larger number of these illnesses and of the more serious involvements occurred among the children given

cod liver oil. The administration of the cod liver oil was interrupted, or rather postponed, because the absences at the hospital all came at the beginning of the year. Moreover, it is doubtful whether those away from the home obtained as good food; in addition, it is rather generally accepted that illnesses of this sort and the accompanying fevers affect all growth and definitely retard development of bone. Stettner⁸ (quoted from Flory¹³) found that "illness caused a cessation in growth and differentiation of the bony framework, the amount of the delay depending on the severity of the disease." In table 8 and in the chart (*E*) are indicated the duration and seriousness of the illnesses in the two matched groups; also, the proportion of the days of illness in each quarter of the experimental year. Several points are to be noted. The total number of days was much larger for the experimental than for the control group, four hundred and twenty as contrasted with two hundred and twenty-seven. The duration of the more serious contagious diseases amounted to two hundred and seventy days for the group given cod liver oil as compared with one hundred and seven for the control group. For both groups a larger portion fell in the first quarter, but again there was more illness for the children taking a supplement, 81 per cent of whose days of illness occurred in March, April and May, as against 54 per cent for the group with the nonsupplemented diet. Table 8 does not show that all the more serious diseases of the group given a supplement occurred during these months, in the first quarter of the year. Illness in the last three quarters included chickenpox, German measles and other mild disorders.

What might be expected under these circumstances? First, if Pryor, Rotch, Stettner, Todd and others were correct in stating that these diseases are nutritional disasters which affect ossification, the bone growth of the group taking cod liver oil might be much more retarded than that of the control group. All 19 experimental subjects had some children's disease, although a few escaped with nothing more serious than chickenpox or German measles. Second, some workers have expressed the belief that vitamin A specifically protects against disease and the damage that may result from it. What seems to be the total result in this case? The first noteworthy fact is that the group given cod liver oil had but 19 per cent of their illness after the first quarter while the control group had 45 per cent. This appears to be evidence for protection by the vitamins. Whether or not the cod liver oil was responsible for the decrease in illness in the experimental group, the second significant fact seems to be that, serious illness notwithstanding, the partners who had the supplement made a definitely larger advance in growth of bone than the control partners, who had less illness. It appears possible that the cod liver oil protected the experimental group from permanent

TABLE 8.—*Number of Children in Each Group Who Were Ill, Number of Days of Illness and Distribution of Illness over the Year, with Indication of Its Seriousness*

Group	Total Number of Children	Children Ill		Total Days of Illness	Days of Illness by Quarter Year												Days of Illness			
		No.	%		1			2			3			4			Diphtheria, Scarlet Fever, Pneumonia		Measles, Whooping Cough	
					March April May	June July August	September October November	December January February	No.	%	No.	%	No.	%	No.	%	No.	%		
Control.....	19	16	84	277	153	55	52	19	48	17	24	9	69	25	38	14				
Cod liver oil..	19	19	100	420	339	81	39	9	28	7	14	3	183	44	87	21				

injury and allowed it, in spite of what might have been nutritional disasters, to make somewhat more than an average gain in bone growth and thus to make up a little of its deficit. The control group, on the other hand, increased its deficit, although it had much less severe and extended illnesses. It seems possible that the two vitamins were a protection for the process of ossification and prevented delay that might have been serious.

COMMENT

It appears that the good diet in this institution was susceptible of improvement. An increase in the amount of vitamins A and D seemed to allow for somewhat better growth of bone than the diet without the increase, and this improvement took place despite the greater duration and severity of the illnesses which the children with cod liver oil had to endure as compared with those of the control children. The diseases concerned—scarlet fever, measles, diphtheria and whooping cough—with their accompanying fever and occasional consequent pneumonia, are known to affect adversely both quality and rate of bone development. Improvement in the ossification of the group given a supplement was accompanied by a greater decrease in the incidence of illness than was noted in the control group for the last three quarters of the year. This may be another indication of improved nutritional status coincident with the superior bone development and related to the supplement.

Two particularly appropriate studies have been reported in which well children have responded to increased amounts of the dietary essentials employed in this study. The cod liver oil increased the amount of vitamins A and D in a diet which, as it contained some of all foods recommended for children's diets, was not known to be deficient in these vitamins. In the case of both vitamin A and vitamin D, however, it has been shown that "well subjects," children who to all outward appearances are in good health, may respond to increased amounts. Blunt and Cowan²⁰ mentioned the fact that more calcium and phosphorus are stored by an infant or young animal given cod liver oil or ultraviolet irradiation than by an untreated companion and that this phenomenon has been noted in well subjects as well as in those with rickets. Sherman cited the findings of Widmark and Svensson,²¹ who gave vitamin A in the form of cod liver oil to children of school age in Malmö, Sweden. Although they found no appreciable difference between control and experimental

20. Blunt, K., and Cowan, R.: *Ultraviolet Light and Vitamin D in Nutrition*. Chicago, University of Chicago Press, 1930.

21. Widmark, E. M. P.: Vitamin A Deficiency in Denmark and Its Results, *Lancet* **1**:1206, 1924. Widmark, E. M. P., and Svensson, B.: Studien über den Bedarf und zur Verfügung stehende Mengen an fettlöslichen Vitaminen der Kinder in den Volksschulen zu Malmö, *Skandinav. Arch. f. Physiol.* **54**:127, 1928: cited by Sherman.²

children in height, weight, hemoglobin content of blood or evidence of night blindness, there was general improvement in health and vitality. Whether or not there had been a noticeable deficit, then, in this institutional diet, increased amounts of these two vitamins might approach the optimum and have a beneficial effect on nutrition and on development of bone.

It has been shown that almost any factor which influences the general nutritional condition has its effect on growth of bone as on all other tissues, though some essentials, such as calcium, may have a more specific function in relation to bone and therefore may have a more prompt effect than others which are less specific, such as energy. Rate of growth is undoubtedly proportional to many factors. Winters, Smith and Mendel²² retarded growth in rats in various ways, with low calory, low protein, low lysine and low salt diets. The greatest modification of the dry weight of the bones took place in the group given a low salt diet and the least in the group given a low energy diet. Smith²³ in his review mentioned the persistence of the growth of bone in all these kinds of retardation of body growth. He referred also to the acceleration noted by Osborne and Mendel when animals were fed an adequate diet after having been stunted for a considerable time by various diets, which were low in protein, lysine, calories or vitamins.

As might be expected, therefore, in 73 children of the previously reported study¹ who received milk and in 37 of the study reported here who received cod liver oil in addition to their regular diet, there was appreciable modification of rate of skeletal development as compared with that of 65 control children. Before further discussion of results it is important to present in combined form the data from the studies on milk and cod liver oil. Comparison may now be made between all of the 110 children of both studies given a supplement and all of the 65 children not given a supplement (table 9). The gains in bone growth made by the children receiving an addition of milk or of cod liver oil to their regular institutional diet are seen to be definitely larger than those made by the children receiving the institutional diet alone. This superiority in growth was shown by every method used in comparing the groups. More than half the children receiving a supplement made their expected gain or more. Twenty-one per cent of them made 150 per cent or more of the gain indicated for their age by the norms. Considerably less than half the control children, 36 per cent, made the average gain or more, and of the 36 per cent only 5 per cent had large gains. Conversely, the larger losses were 10 and 18 per cent for the experimental

22. Winters, J.; Smith, A. H., and Mendel, L. B.: The Effects of Dietary Deficiencies on the Growth of Certain Body Organs, *Am. J. Physiol.* **8**:576, 1927.

23. Smith, A. H.: Phenomena of Retarded Growth, *J. Nutrition* **4**:427, 1931.

and the control groups, respectively. Forty-two per cent of the children given a supplement were in a more favorable relation to the mean for their age than at the beginning of the year as against 27 per cent of those without supplement. The larger number of the large gains (5 or more points) were made by the experimental group, 14.5 per cent, in contrast to 5 per cent for the control group, and the larger number of large losses by the control group, 20 per cent, in contrast to 7 per cent for the experimental group. The control children as a group made 85

TABLE 9.—*Progress in Bone Growth of the One Hundred and Eight Children of the Study on Milk, and of the Sixty-Seven Children of the Study on Cod Liver Oil*

Item	Control Group	Experimental Group
Number of children.....	65	110
Percentage of children even with or above mean:		
Beginning.....	29	26
End.....	23	26
Percentage of children 10% or more below mean:		
Beginning.....	46	46
End.....	47.7	41
Percentage of children in more favorable relation to mean by 5% or more.....	17	29
Percentage of children in less favorable relation to mean by 5% or more.....	23	11
Percentage of expected gain.....	85 $\pm$ 3.83	113.0 $\pm$ 4.18
Percentage of children making expected gain or more.....	36	54.5
Less than 50%.....	18	10
150% or more.....	5	22

TABLE 10.—*Statistical Summary: Comparison of Partners*

Set of Partners Compared	Pairs	Mean of Differences Between Partners	Difference Probable Error	Probability of Difference Being Due to Supplement
Partners receiving milk				
Plain vs. control.....	24	2.71 $\pm$ 0.84	3.2	33 to 1
D milk vs. control.....	24	2.67 $\pm$ 0.77	3.5	55 to 1
Plain vs. D milk.....	24	0.04 $\pm$ 0.90	...	
Partners receiving cod liver oil				
Cod liver oil vs. control.....	19	1.63 $\pm$ 0.55	3.0	23 to 1
All partners receiving milk or cod liver oil				
Experimental vs. control.....	67	2.37 $\pm$ 0.44	5.4	3,000 to 1

per cent of the total gain in ossification to be expected, and the children given milk and cod liver oil, 113 per cent of their quota. The difference between these figures (28 ± 5.7) is statistically significant. The difference divided by its probable error is 4.9, which means that the chances are about 1,000 to 1 that the difference is not due to chance (table 11).

There is a further, more precise, comparison to be made, which concerns the 67 sets of partners (table 10). It will be seen here that the average difference between partners in these 67 sets is 2.37 ± 0.44 ; the difference divided by its probable error is 5.4. This indicates that

TABLE 11.—*Statistical Summary: Comparison of All Groups in Studies on Cod Liver Oil and Milk as to Percentages of Expected Gain*

Groups Compared		No. in Control Group	No. in Experi- mental Group	M ₁	M ₂	P. E. of M ₁ — M ₂	Diff. P. E.	Probability Difference Is Not Due to Chance
Cod liver oil vs. control group								
Matched groups								
		19	19	105.2 ± 5.02	86.9 ± 4.99	18.3 ± 7.08	2.6	13 to 1
All children in larger home		23	29	101.6 ± 4.20	85.5 ± 4.72	16.1 ± 6.32	2.5	12.5 to 1
All children given cod liver oil		30	37	95.8 ± 3.98	80.7 ± 3.96	15.1 ± 5.61	2.7	14.6 to 1
Milk Groups								
Matched								
Plain vs. control		24	24	124.0 ± 10.6	78.0 ± 6.3	46.0 ± 12.4	3.7	79 to 1
D milk vs. control		24	24	118.0 ± 8.4	78.0 ± 6.3	40.0 ± 10.5	3.8	96 to 1
Plain vs. D milk		24	24	124.0 ± 10.6	118.0 ± 8.4	6.0 ± 13.5	0.4	
Total								
Plain vs. control		35	37	128.0 ± 8.96	87.5 ± 6.40	40.5 ± 11.0	3.7	79 to 1
D milk vs. control		35	36	120.3 ± 7.67	87.5 ± 6.40	32.8 ± 10.0	3.3	38 to 1
Plain vs. D milk		37	36	128.0 ± 8.96	120.3 ± 7.67	7.7 ± 12.0	0.6	
All subjects given milk or cod liver oil		65	110	113.0 ± 4.18	85.0 ± 3.53	28.0 ± 5.67	4.9	1,111 to 1

the chances are 3,000 to 1 that this difference is not due to chance and therefore that it may reasonably be ascribed to the experimental procedure.

The data from both studies seem to point to a definite relation between the increase in rate of bone growth and the improvement of the diets by the supplements. A greater change in rate occurred in the case of milk, which removed a larger deficiency, and a smaller change, as might be expected, in the case of cod liver oil, which was added to a diet with no great deficiency. In each case there is reason to believe the results significant, because they are consistently in favor of the groups given a supplement. When the data from the two studies are combined, each set fortifies the other, and the two give definitely significant results. The study as a whole, then, yields data supporting the impression of a number of workers in this field that nutrition directly influences bone growth and that it does so quantitatively as well as qualitatively.

SUMMARY

Roentgenograms of the right hands and forearms of 67 children were taken at the beginning and end of a calendar year, and the progress in development of bone, as indicated by changes in the Carter ossification ratio, was followed. Half of the children were kept on the institutional diet as controls; half were given in addition a daily dessertspoonful of cod liver oil. The most valuable comparisons are those made for 19 pairs, each made up of a control and an experimental partner, who were matched at the beginning for sex and stage of bone development.

By all methods of comparison the group given a supplement showed somewhat greater progress than did the control group. The differences were all in the same direction, in favor of the children taking cod liver oil, although in the first quarter of the experimental year this group had two hundred and seventy days of illness with the more serious childrens' diseases, which are known to affect quality and quantity of bone growth. The control group had one hundred and seven days of similar illness. Although approximately one third of each group were retarded in respect to the Carter norms and were still retarded at the end of the study, the group given a supplement reduced, and the group without a supplement somewhat increased, their deficits. This is shown by the following summary:

1. The percentage of children in more favorable relation to the Carter standard for age at the end than at the beginning of the year was 32 for the control group and 42 for that given cod liver oil.
2. The control group as a whole gained 86 per cent and the group taking cod liver oil 104 per cent of its expected quota.

3. In the control group 47.5 per cent of the children gained the amount to be expected of them or more, while in the group given cod liver oil 58 per cent made such a gain.

4. In the 19 pairs the control child made the best gain in 5 (26 per cent) and the child receiving cod liver oil in 12 (63 per cent) of the comparisons. The amount of the superiority is shown in a comparison of the partners in the pairs as to variation from expected gain, the most accurate test of the result. By this method the mean advantage of the children in the group taking cod liver oil over their control partners was found to be 1.63 ± 0.55 points. As the relation of this difference to its probable error is 3, the advantage is probably significant.

5. The addition of a dessertspoonful of cod liver oil to an institutional diet every day for eight to twelve months of a year seemed to be a factor of safety and may have been a protection for the process of bone growth. This institutional diet, good as it appeared to be, was apparently susceptible of improvement.

When data from studies on both milk and cod liver oil are combined and the growth of bone of 110 children who were receiving a supplement is compared with that of 65 children who were not, the contrast between the groups is increased. The percentage of children in a more favorable relation to the Carter norm for age at the end than at the beginning is 27 for the group without the supplement and 42 for the group with it; the control group as a unit gained 85 per cent and the experimental group 113 per cent of its expected quota; in the control group 36 and in the experimental group 55 per cent of the children gained 100 per cent or more of the amount to be expected of them. In the 67 comparisons of matched partners the mean superiority of children given a supplement over their partners, who had none, was 2.37 ± 0.44 . This difference is significant, as its relation to its probable error is 5.4.

Evidence has been presented to show that the rate of bone development in the wrist is related to the diet of the child. Supplements to institutional diets, a daily pint of reconstituted evaporated milk or a dessertspoonful of cod liver oil, have seemed to be a protection for the process of bone growth, for the children who were receiving them made somewhat better gains than those who were not.

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Department of Home Economics, Winthrop College.

